REMARKS

Claims 1-8, 10, 11, and 43-45 are pending in the instant application. Claims 2 and 3 have been amended. Support for the amendments to the claims can be found in the specification at, for example, page 93, lines 15-18 and lines 23-27; page 95, lines 14-16; Example 3; and Example 5. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejections of claims 1-8, 10, 11, and 43-45 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1, 2, 4-8, 10, 11, and 43-45 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that while the claimed invention encompasses allelic variants, which have particular sequences, the specification does not set forth these sequences, and there is no other way to identify these sequences.

Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that is at least about 70 percent identical to the polypeptide set forth in SEQ ID NO: 5; a region of the nucleotide sequence of SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-976, or the nucleotide sequence above, encoding a polypeptide fragment of at least about 25 amino acid residues; a region of the nucleotide sequence of SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-976, or either of the nucleotide sequences above, comprising a fragment of at least about 16 nucleotides; a nucleotide sequence that hybridizes to the complement of any of the nucleotide sequences above under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences; or a nucleotide sequence that is complementary to the nucleotide sequence of any of the nucleic acid molecules above. Applicants contend that because claim 2, as amended, no longer recites an isolated nucleic acid molecule comprising a nucleotide sequence encoding an allelic variant of the nucleotide sequence set forth in SEQ ID NO: 4 or of the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-976, amended claim 2 satisfies the requirements of 35 U.S.C. § 112, first paragraph.

The instant Office Action maintains the rejection of claims 1-8, 10, 11, and 43-45 under 35

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U.S.C. § 112, first paragraph, as lacking enablement commensurate with the scope of the claims. The Office Action mailed August 24, 2001 asserted a rejection of claims 1-8, 10, 11, and 43-45 as not being enabling for certain claimed IFN-L variants. That Action stated that because no particular biological activity for IFN-L is set forth in the specification, one of ordinary skill in the art would not be able to make IFN-L variants possessing the same activity as INF-L. The Office Action mailed May 16, 2002 maintained this rejection, stating that the claimed IFN-L variants are not limited to any particular activity and that the specification contains no definition of "an activity of the polypeptide set forth in SEQ ID NO: 5." That Action also stated that, in the absence of guidance as to a particular functional activity or structural elements required for function, it would require undue experimentation for one of ordinary skill in the art to make and use the invention as claimed. The instant Action maintains this rejection, stating that because tyrosine phosphorylation of cellular proteins occurs in response to many different stimuli, the requirement that the claimed IFN-L variants cause an increase in the tyrosine phosphorylation of cellular proteins, rather than particular molecules associated with signaling, does not provide a particular functional limitation. The instant Action also states that because antigenicity is not a particular property of interferons, the limitation that certain claimed IFN-L variants be antigenic also does not provide a particular function limitation.

Applicants respectfully disagree with the Action's assertion that claims containing the limitation of antigenicity (*i.e.*, claim 2(b)) are not enabled commensurate with their full scope. Applicants note that the instant application teaches the nucleotide and amino acid sequences of human IFN-L (Figures 2A-2B; SEQ ID NO: 4 and SEQ ID NO: 5) and that a deposit of cDNA encoding human IFN-L, having Accession No. PTA-976, was made with the American Type Culture Collection (page 92, lines 25-28) under the provisions of the Budapest Treaty. Applicants contend that based on the specification's teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to determine which IFN-L polypeptide fragments of at least about 25 amino acid residues are antigenic. Nevertheless, in an effort to expedite prosecution of the pending claims to allowance, Applicants have amended claim 2(b) so that it is directed to polypeptide fragments that are capable of specifically binding an interferon receptor, thereby resulting in an increase in the tyrosine phosphorylation of a Janus kinase protein. Applicants, having deleted the objected-to limitation of antigenicity, contend that this ground of

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rejection has been overcome. Withdrawal of this rejection is therefore respectfully requested.

Applicants also respectfully disagree with the Action's assertion that claims containing the limitation that an IFN-L variant, upon exposure to mammalian cells, cause an increase in cellular protein tyrosine phosphorylation (*i.e.*, claims 2(a)-(c) and 3(a)-(e)) are not enabled commensurate with their full scope. Applicants note that the instant application teaches that the nucleotide sequence of human IFN-L shares the characteristic intronless structure of the interferon gene family (page 93, lines 23-27), that the disclosed nucleotide sequence of rat IFN-L shares amino acid sequence homology with members of the interferon family of proteins (page 93, lines 15-18), that human and rat IFN-L are secreted cytokines (page 95, lines 14-16) which share conserved cysteine residues with IFN-β (Figure 3), and that cells exposed to a rat IFN-L-Fc fusion protein show an increase in cellular protein tyrosine phosphorylation (page 103, lines 19-27). Applicants contend that in the view of the specification's teachings, one of ordinary skill in the art would recognize that the instant specification discloses a novel member of the interferon family of proteins.

Applicants also note that at the time the instant application was filed, it was well established in the art that interferon-mediated signal translation involves interferon cell-surface receptors, members of the Janus kinase (JAK) protein family, and cytoplasmic transcription factors known as STATs (signal transducers and activators of transcription). Interferon-mediated signal translation is initiated by the binding of a member of the interferon family of proteins to an interferon cell-surface receptor (Silvennoinen *et al.*, 1993, *Nature* 366:583-85). The binding of an interferon molecule to its cell-surface receptor induces rapid tyrosine phosphorylation of the receptor itself as well as the activation, by tyrosine phosphorylation, of a member of the JAK protein family (*e.g.*, JAK1, JAK2, or tyk2) (Silvennoinen *et al.*, 1993; Ihle, 1994, *Proc. Soc. Exp. Biol. Med.* 206:268-72; Colamonici *et al.*, 1994, *Mol. Cell. Biol.* 14:8133-42). Activated JAK proteins then activate, by tyrosine phosphorylation, members of the STAT family of proteins, which translocate to the nucleus to direct transcriptional activation. (Ihle, 1994; Shuai, 1994, *Curr. Opin. Cell Biol.* 6:253-59). Therefore, at the time the instant application was filed, one of ordinary skill in the art, based on the knowledge in the art, would have appreciated that the binding of an interferon molecule to its cell-surface receptor would initiate interferon-mediated signal translation, resulting in the tyrosine phosphorylation of interferon cell-surface receptor, JAK, and STAT proteins – and thus an increase in cellular tyrosine phosphorylation.

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Applicants contend, therefore, that contrary to the assertion made in the instant Action, the requirement that the claimed IFN-L variants cause an increase in cellular protein tyrosine phosphorylation provides a particular functional limitation, and that based on the specification's teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to determine which IFN-L polypeptide variants cause an increase in cellular tyrosine phosphorylation. Applicants also contend that because claims 2(a)-(c) and 3(a)-(e) (*i.e.*, claims containing this limitation) also contain additional sequence-related limitations, these claims are enabled commensurate with their full scope. Moreover, Applicants contend that it would be improper to view the limitation that the claimed IFN-L variants cause an increase in cellular protein tyrosine phosphorylation *apart* from the sequence-related limitations in the claims. For example, while one of ordinary skill in the art might readily be able to identify a nucleic acid molecule encoding a polypeptide that causes an increase in cellular protein tyrosine phosphorylation, Applicants contend that the skilled artisan would be extremely unlikely to identify a nucleic acid molecule that encodes a polypeptide sharing at least about 70% sequence identity to the polypeptide forth in SEQ ID NO: 5 *and* which causes an increase in cellular protein tyrosine phosphorylation. This is illustrated in Appendix A, which shows the results of a recent BLAST search using the polypeptide of SEQ ID NO: 5. Of the fifty sequences identified in this search as sharing the highest degree of sequence identity with the polypeptide of SEQ ID NO: 5, only *two* sequences (GenBank Accession Nos. NP_064509.1, published April 6, 2003, human IFN-κ precursor; and AAK63834.1, published October 23, 2001, rat IFN-κ precursor) were found to share at least 70% identity with the polypeptide of SEQ ID NO: 5, and each of these polypeptides appears to be a member of the interferon family. None of the remaining sequences identified in the search were found to share more than 37% identity with the polypeptide of SEQ ID NO: 5, let alone belong to a family known to cause an increase in cellular protein tyrosine phosphorylation. Applicants note that GenBank Accession Nos. NP_064509.1 and AAK63834.1 were published subsequent to Applicants' identification of the nucleic acid and amino acids sequences for IFN-L polypeptide, and indeed, after Applicants' priority filing date of December 8, 1999, and therefore, that neither reference is prior art to the instant application under 35 U.S.C. § 102.

Despite Applicants' contention that claims containing the limitation that the claimed IFN-L variants cause an increase in cellular protein tyrosine phosphorylation are fully enabled, in an effort

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to expedite prosecution of the pending claims to allowance Applicants have amended claims 2(a)-(c) and 3(a)-(e) to recite that the claimed IFN-L variants are capable of specifically binding an interferon receptor, thereby resulting in an increase in the tyrosine phosphorylation of a Janus kinase protein. Applicants contend that at the time the instant application was filed, it was well established in the art that an increase in *cellular* protein tyrosine phosphorylation detected following the exposure of an IFN-L variant to mammalian cells was merely the result of an increase in the tyrosine phosphorylation of interferon cell-surface receptors, JAKs, and STATs. Applicants contend, therefore, that the claims, as amended, are directed to IFN-L variants having a characteristic interferon activity, and that the instant specification when coupled with the knowledge in the art at the time the instant application was filed, teach the skilled artisan how to make and use the claimed invention without undue experimentation. Withdrawal of this ground of rejection is therefore respectfully solicited.

The instant Office Action also maintains the rejection of claims 1-8, 10, 11, and 43-45 under 35 U.S.C. § 112, first paragraph, as lacking written description. The Office Action mailed August 24, 2001 asserted a rejection of claims 1-8, 10, 11, and 43-45 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. That Action stated that the disclosure of two nucleic acid sequences does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. That Action noted that a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus *or* a recitation of structural *or* functional features common to the members of the genus. The Office Action mailed May 16, 2002 maintained this rejection, stating that the claims are drawn to molecules having "an activity of the polypeptide set forth in SEQ ID NO: 5," rather than a phosphorylation activity and that the specification contains no definition of phosphorylation activity. That Action also stated that because phosphorylation is not specific to any particular molecule or class of molecules, phosphorylation is not an activity that defines a genus of IFN-L molecules. The instant Action maintains this rejection, stating that while the specification discloses a general increase in the tyrosine phosphorylation of cellular proteins, the characteristic phosphorylation activity of interferons involves the tyrosine phosphorylation of particular molecules associated with

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signaling (*i.e.*, Janus kinases). The instant Action also states that antigenicity is not a particular characteristic of interferons.

As discussed above, it was well established in the art at the time the instant application was filed that an increase in cellular protein tyrosine phosphorylation could be detected following the exposure of an interferon molecule to a mammalian cell, and that such an observation would be due to the increase in interferon cell-surface receptor, JAK, and STAT tyrosine phosphorylation. To expedite prosecution of the instant application, Applicants have amended claims 2(a)-(c) and 3(a)-(e) to recite that the claimed IFN-L variants are capable of specifically binding an interferon receptor, thereby resulting in an increase in the tyrosine phosphorylation of a Janus kinase protein. Applicants contend that the explicit disclosure in the specification that the IFN-L polypeptides of the invention possess the ability to increase cellular protein tyrosine phosphorylation (Example 5) coupled with the knowledge in the art at the time the instant application was filed that interferon-mediated signal translation results in the tyrosine phosporylation of cell-surface receptors, JAKs, and STATs provides support for this limitation. Applicants also contend that because the amended claims recite a characteristic functional feature common to the members of the genus of claimed IFN-L polypeptides, the claims satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Withdrawal of this ground of rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Andres believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

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Respectfully submitted,
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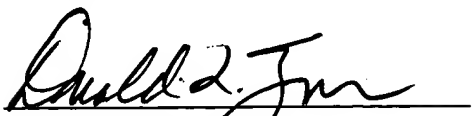
By: 
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EXHIBIT A

Sequences producing significant alignments:	Score (bits)	E Value
gi|23110976|ref|NP_064509.1| interferon kappa precursor; in...	**344**	**4e-94**
gi|14488026|gb|AAK63834.1|AF384047_1 interferon kappa precu...	**290**	**1e-77**
gi|27714381|ref|XP_232873.1| similar to interferon kappa pr...	104	7e-22
gi|31076541|gb|AAP43908.1| interferon kappa precursor [Mus ...	94	9e-19
gi|625506|pir||A61403 interferon alpha-II-10 precursor - sheep	85	8e-16
gi|585317|sp|P37290|IND1_HUMAN Interferon delta-1 precursor...	84	1e-15
gi|27819618|ref|NP_776776.1| interferon, omega 1 [Bos tauru...	84	2e-15
gi|2136874|pir||I46397 interferon alpha - sheep >gi|416542|...	83	3e-15
gi|6707689|sp|O46633|INT_CEREL INTERFERON TAU PRECURSOR (IF...	83	3e-15
gi|2118659|pir||I47070 interferon omega - sheep >gi|165829|...	82	4e-15
gi|4504605|ref|NP_002168.1| interferon, omega 1 [Homo sapie...	82	6e-15
gi|1708490|sp|P49876|INAF_BOVIN Interferon alpha-F precurso...	80	3e-14
gi|124430|sp|P07348|INA1_BOVIN Interferon alpha-1 precursor...	80	3e-14
gi|108329|pir||S23711 interferon alpha-II-5 precursor - pig...	79	3e-14
gi|758083|emb|CAA26501.1| human interferon omega precursor ...	79	3e-14
gi|386800|gb|AAA52724.1| interferon-alpha ...	79	6e-14
gi|6707694|sp|P28169|INTB_SHEEP INTERFERON TAU-11 PRECURSOR...	78	8e-14
gi|847816|gb|AAA70091.1| interferon omega-1 ...	78	1e-13
gi|478668|pir||S23710 interferon alpha-II-4 precursor - pig...	77	1e-13
gi|10180643|gb|AAG14170.1| interferon tau [Bos taurus]	77	1e-13
gi|124450|sp|P05008|INAB_BOVIN Interferon alpha-B precursor...	77	1e-13
gi|124454|sp|P05010|INAD_BOVIN Interferon alpha-D precursor...	77	2e-13
gi|4504603|ref|NP_002167.1| interferon, beta 1, fibroblast ...	77	2e-13
gi|20178265|sp|P01570|INAD_HUMAN Interferon alpha-14 precur...	75	5e-13
gi|1708492|sp|P49878|INAH_BOVIN Interferon alpha-H precurso...	75	7e-13
gi|124434|sp|P05004|INA2_HORSE Interferon alpha-2 precursor...	75	7e-13
gi|69659|pir||IVHUA9 interferon alpha-17 precursor - human ...	75	8e-13
gi|1708491|sp|P49877|INAG_BOVIN Interferon alpha-G precurso...	74	1e-12
gi|10880985|ref|NP_067091.1| interferon, alpha 17 [Homo sap...	74	1e-12
gi|3766295|emb|CAA09862.1| interferon beta [Macaca fascicul...	74	1e-12
gi|4504591|ref|NP_002163.1| interferon, alpha 14 [Homo sapi...	74	1e-12
gi|124499|sp|P05001|INO1_HORSE Interferon omega-1 precursor...	74	1e-12
gi|2118648|pir||I37584 IFN-alpha-N-protein - human >gi|3272...	74	1e-12
gi|7558588|gb|AAC60525.2| interferon-omega48; IFN-omega48 [...	74	2e-12
gi|28882045|ref|NP_795372.1| interferon tau-1 [Homo sapiens...	73	2e-12
gi|27806581|ref|NP_776510.1| interferon, alpha, leukocyte [...	73	3e-12
gi|124447|sp|P05007|INAA_BOVIN Interferon alpha-A precursor...	73	3e-12
gi|2118660|pir||I51970 interferon precursor - human >gi|186...	72	4e-12
gi|124431|sp|P05003|INA1_HORSE Interferon alpha-1 precursor...	72	4e-12
gi|2118661|pir||I56314 interferon-alpha - human (fragment) ...	72	4e-12
gi|124437|sp|P05006|INA4_HORSE Interferon alpha-4 precursor...	72	5e-12
gi|124436|sp|P05005|INA3_HORSE Interferon alpha-3 precursor...	72	5e-12
gi|2147610|pir||I46972 interferon-omega44 - rabbit >gi|5451...	72	6e-12
gi|4504593|ref|NP_002164.1| interferon, alpha 16 [Homo sapi...	72	6e-12
gi|2136876|pir||S70011 interferon type I precursor - sheep ...	72	8e-12
gi|27715055|ref|XP_233163.1| similar to Interferon alpha-1 ...	71	9e-12
gi|108328|pir||S23712 interferon alpha-II-3 precursor - pig...	71	1e-11
gi|1708489|sp|P49879|INA1_PIG Interferon alpha-1 precursor ...	71	1e-11
gi|2136875|pir||I46398 interferon alpha - sheep >gi|1197|em...	71	1e-11
gi|184623|gb|AAC41702.1| interferon-beta	71	1e-11